

Translation

PATENT COOPERATION TREATY

RECEIVED

MAY 24 2002

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT CENTER 1600/2900

(PCT Article 36 and Rule 70)

| | | |
|--|---|---|
| Applicant's or agent's file reference LTS 1999/017 PCT | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
| International application No. PCT/EP00/07904 | International filing date (day/month/year) 14 August 2000 (14.08.00) | Priority date (day/month/year) 27 August 1999 (27.08.99) |
| International Patent Classification (IPC) or national classification and IPC A61K 9/51, 47/48 | | |
| Applicant LTS LOHMANN THERAPIE-SYSTEME AG | | |

| |
|---|
| 1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36. |
| 2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet. |
| <input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). |
| These annexes consist of a total of <u>4</u> sheets. |
| 3. This report contains indications relating to the following items: |
| I <input checked="" type="checkbox"/> Basis of the report |
| II <input type="checkbox"/> Priority |
| III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| IV <input type="checkbox"/> Lack of unity of invention |
| V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| VI <input type="checkbox"/> Certain documents cited |
| VII <input checked="" type="checkbox"/> Certain defects in the international application |
| VIII <input checked="" type="checkbox"/> Certain observations on the international application |

| | |
|--|--|
| Date of submission of the demand 07 March 2001 (07.03.01) | Date of completion of this report 15 November 2001 (15.11.2001) |
| Name and mailing address of the IPEA/EP | Authorized officer |
| Facsimile No. | Telephone No. |

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP00/07904

I. Basis of the report

1. With regard to the elements of the international application:*

 the international application as originally filed the description:

pages _____ 1-6 _____, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

 the claims:

pages _____, as originally filed

pages _____, as amended (together with any statement under Article 19) _____, filed with the demand

pages _____, filed with the letter of _____

1-14, filed with the letter of 18 September 2001 (18.09.2001)

 the drawings:

pages _____, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

 the sequence listing part of the description:

pages _____, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

 the language of a translation furnished for the purposes of international search (under Rule 23.1(b)). the language of publication of the international application (under Rule 48.3(b)). the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

 contained in the international application in written form. filed together with the international application in computer readable form. furnished subsequently to this Authority in written form. furnished subsequently to this Authority in computer readable form. The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished. The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. The amendments have resulted in the cancellation of: the description, pages _____ the claims, Nos. _____ the drawings, sheets/fig _____5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP 00/07904

I. Basis of the report

1. This report has been drawn on the basis of (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

The submitted amendments are consistent with PCT Article 34(2) (b).

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP00/07904

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|-------------------------------|--------|------|-----|
| Novelty (N) | Claims | 1-14 | YES |
| | Claims | | NO |
| Inventive step (IS) | Claims | 1-14 | YES |
| | Claims | | NO |
| Industrial applicability (IA) | Claims | 1-14 | YES |
| | Claims | | NO |

2. Citations and explanations

Reference is made to the following documents:

D1: WO 99/36090 A, HUANG SHAU KU; LEONG KAM W. (US);
ROY KRISHNENDU (US); SAMPSON HUGH, 22 July 1999
(1999-07-22)

D2: WO 97/47323 A, ZONAGEN INC., 18 December 1997
(1997-12-18)

D3: EP-A-0 860 166, UNIV. SANTIAGO COMPOSTELA,
26 August 1998 (1998-08-26).

A solid pharmaceutical preparation is claimed in Claim 1, comprising an at least partially charged active ingredient in the form of a nanosol, in which the active ingredient is bonded to a negatively charged chitosan derivative, produced by a given method.

D1, considered to be the closest prior art, relates to pharmaceutical preparations containing a chitosan derivative combined with the pharmaceutical and produced by coacervation. D1 differs from the application in that chitosan derivative and the active ingredient are not

/...

precipitated by adjustment of the pH value which allows an isoionic state to be achieved. The technical problem was that of devising a pharmaceutical preparation without gelatine for charged active ingredients in which the active ingredient is present in an oppositely-charged carrier. Said problem is solved by means of a preparation produced by means of a given method.

D2 relates to a method in which a metal salt is added to the chitosan derivative, the metal from which can become an integral constituent of the chitosan particles. D3 describes a method in which an ionic cross-linking agent is used. The above solution is not obvious for an expert in the field since it cannot be derived from the prior art that, by adjusting the pH value in the aqueous sol, which already contains chitosan particles, and thereby achieving an isoionic state between chitosan particles and active ingredient, nano-scale particles of the active ingredient can be precipitated in order to produce pharmaceutical preparations in the manner described.

For this reason, Claims 1-14 involve an inventive step (PCT Article 33(3)).

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP00/07904

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Contrary to PCT Rule 5.1(a)(ii), the description does not cite D1 to D3 or indicate the relevant prior art disclosed therein.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP00/07904

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

In Claim 4, the relative term "almost" has no generally accepted meaning and leaves the reader unclear as to the meaning of the relevant technical features. In consequence, the definition of the subject matter of said claim lacks clarity.

In Claim 7, part of the text has been omitted (PCT Article 6).